

CLAIMS

1. Process for the preparation of a nucleic acid by synthesis on a solid support, characterized in that an inorganic or organic polymer is used as solid support, 5 which polymer is connected via a divalent hydrocarbon radical to an epoxide group or a group of the glycol type, the latter group consisting of two adjacent saturated carbons on which an OH group and a nucleophilic group are respectively substituted.

10 2. Process according to Claim 1, characterized in that the first nucleotide is advantageously attached to the solid support under the same conditions and with the same monomer reagent as for the condensation of the second nucleotide with the first nucleotide bonded to the 15 support, which may be the conventional conditions and monomer reagent used during the synthesis of nucleic acids on a solid support, the said first nucleotide corresponding to the first nucleotide in the sequence of the said nucleic acid.

20 3. Process according to either of Claims 1 and 2, characterized in that it comprises the following steps of:

1) condensation of the 5' or 3' OH group of the first 25 nucleotide or of an oligonucleotide connected at its other 3' or 5' end to the said solid support, using a coupling agent, with the phosphate group optionally substituted in the 3' or 5' position respectively of a monomer nucleotide reagent protected in the 3' and 5' positions;

30 2) oxidation or sulfurization of the internucleotide bond of the phosphite type obtained in step 1) to a phosphate or phosphorothioate bond respectively.

35 3) deprotection of the 5'-O or 3'-O end of the product obtained in step 2);

4) repetition of steps 1) to 3) as many times as there are nucleotides to be added in order to synthesize the nucleic acid.

4. Process according to either of Claims 1 and 2, characterized in that it comprises the following steps

of:

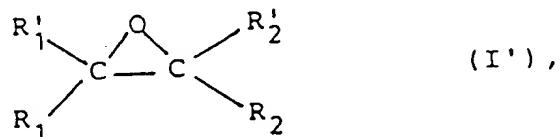
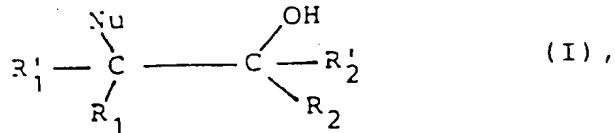
- 1) condensation, using a coupling agent, of the said OH group of the said group of glycol type of the solid support with a phosphate or phosphite group optionally substituted in the 3' or 5' position of a monomer nucleotide reagent protected in the 5'-O and 3-O positions;
- 2) oxidation or sulfurization of the covalent bond of the phosphite type between the solid support and the first nucleotide obtained in step 1);
- 3) deprotection of the 5'-O or 3'-O end of the product obtained in step 2);
- 4) condensation of the 5'OH or 3'OH group of the product obtained in step 3) with the phosphate, phosphorothioate or phosphite group optionally substituted in the 3' or 5' position of a monomer nucleotide reagent protected in the 5'-O or 3'-O position respectively, using the said coupling agent, under the same conditions as the condensation in step 1);
- 5) oxidation or sulfurization of the internucleotide grouping of the phosphite phosphite [sic] type resulting from the above step into a grouping of the phosphate or phosphorothioate type respectively;
- 6) deprotection of the 5'-O or 3'-O end of the product obtained in step 5);
- 7) repetition of steps (4), (5) and (6) as many times as there are nucleotides to be added in order to obtain the nucleic acid to be prepared.

30 5. Process according to Claim 4, characterized in that it includes a final step of detachment of the nucleic acid from the support and removal of the protecting groups from the bases and, where appropriate, from the 2'-O positions of the nucleic acids.

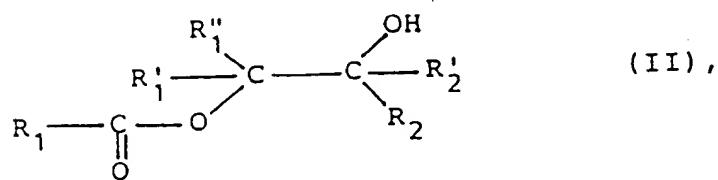
35 6. Process according to either of Claims 4 and 5, characterized in that it comprises a prior step of opening of the said epoxide group of the said solid support, in an anhydrous acidic medium, under the usual conditions for the deprotection of the 5' or 3' OH groups

in order to give the said group of the glycol type of the solid support.

7. Compounds represented by the following formulae:



or



in which:

5 - one of R_1 , R'_1 , R''_1 , R_2 and R'_2 , represents an inorganic or organic polymer or a hydrocarbon radical substituted with an inorganic or organic polymer, and

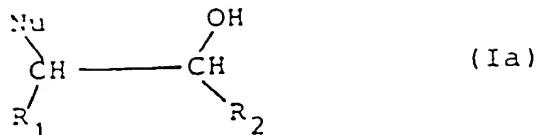
10 the others are identical or different and represent, independently of each other, H or an inert group such as an alkyl group which is optionally substituted, in particular with one or more halogen(s),

15 - Nu represents a nucleophilic group such as NH_2 , Halogen -OAlk, -SAlk, -NHAalk, -NHAac, -OAc, -SAc or - $\text{N}(\text{Alk})_2$, where Alk and Ac respectively represent an alkyl and acyl group, which is optionally substituted, in particular with one or more halogen(s).

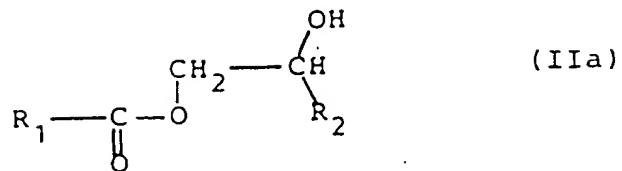
8. Compounds according to Claim 7, characterized in
20 that Nu represents $-\text{N}(\text{Alk})_2$, $-\text{NHAac}$, $-\text{OAc}$, $-\text{SAc}$ or a halogen, where Alk and Ac respectively represent a C_1 to C_4 alkyl and acyl group optionally substituted with one or more halogen(s).

9. Compounds according to Claim 7 or 8, characterized in that the said solid support corresponds to one

of the formulae:

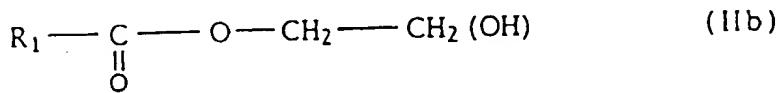
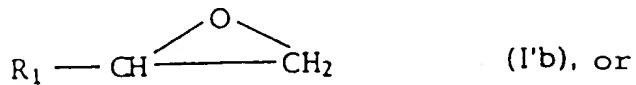
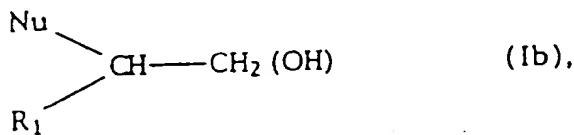


or



in which R_1 , R_2 and Nu have the meanings given in Claim 7.

10. Compound according to Claim 9, characterized in
that the said compound corresponds to one of the formu-
5 lae:



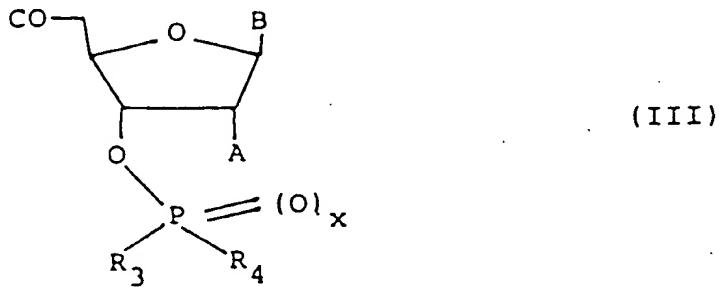
11. Compound according to one of Claims 7 to 9,
characterized in that $(\text{R}_1$ and R_2) or $(\text{R}'_1$ and R'_2) together
form a ring, in particular a heterocycle, on which the
polymer is found substituted.

10 12. Composition according to Claim 11, characterized
in that $(\text{R}_1$ and R_2) or $(\text{R}'_1$ and R'_2) together form a ribose
ring and Nu represents the $2'-\text{O}$ function protected with
a protecting group such as $\text{CH}_3 - \text{C} - \text{O}$.

13. Process according to one of Claims 1 to 6,
15 characterized in that the said solid support consists of
a compound according to one of Claims 7 to 10.

a compound according to one of Claims 7 to 10.

14. Process according to one of Claims 2 to 6 and 13, characterized in that the said nucleotide monomer reagent corresponds to the formula:



5 in which:

- A represents H or an optionally protected hydroxyl group,
- B is a purine or pyrimidine base whose exocyclic amine function is optionally protected,
- 10 - C is a conventional protecting group for the 5'-OH function,
- x = 0 or 1, with

a) when x = 1:

- 15 R₃ represents H and R₄ represents a negatively charged oxygen atom, or
- R₃ is an oxygen atom and R₄ represents either an oxygen atom or an oxygen atom bearing a protecting group, and

- 20 b) when x = 0, R₃ is an oxygen atom bearing a protecting group and R₄ is either a halogen or a disubstituted amine group.

- 15. Process according to Claim 14, characterized in that it is a phosphoramidite synthesis process in which the monomer reagent corresponds to the formula (III) with
- 25 x = 0, R₃ is an oxygen atom bearing a protecting group and R₄ is a disubstituted amine group.

- 16. Process according to one of Claims 1 to 6 and 13 to 15, characterized in that the polymer is in the form of glass microbeads or microfibers, in particular porous ones, silica, metal oxides, cellulose or organic polymer, in particular cellulose.

17. Process according to one of Claims 1 to 6 and 13 to 16, characterized in that the polymer is an inorganic polymer made, in particular, of a glass or silica base.

